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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/063,713	05/08/2002	Dan L. Eaton	P3230R1C001-168	8612

30313 7590 01/13/2005

KNOBBE, MARTENS, OLSON & BEAR, LLP  
2040 MAIN STREET  
IRVINE, CA 92614

EXAMINER

KAUFMAN, CLAIRE M

ART UNIT	PAPER NUMBER
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1646

DATE MAILED: 01/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Applicati n No.

10/063,713

Applicant(s)

EATON ET AL.

Examin r

Claire M Kaufman

Art Unit

1646

-- Th MAILING DATE of this communication appears on th cover sh et with th correspondenc address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 08 May 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-20 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 08 May 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 9/17/02.
- ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: \_\_\_\_\_.

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## DETAILED ACTION

### *Claim Rejections - 35 USC §§ 101/112, First Paragraph*

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-20 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

The claims are drawn as narrowly to a nucleic acid comprising SEQ ID NO:81 or as broadly to a nucleic acid at least 80% identical to a nucleic acid encoding an extracellular domain of SEQ ID NO:82. The specification asserts a number of utilities for the encoding nucleic acid, however, these utilities are not specific and substantial or well established. The encoding nucleic acid cannot derive a utility from the encoded polypeptide because there is neither a known physiological or clinical significance of the polypeptide, and the prior art does not support a very close structural relationship to a well described (structurally and functionally) family of known proteins.

An asserted utility is in drug screening and rational drug design. The method involves screening for “agents which can affect a PRO polypeptide-associated disease or disorder” (p. 135, ¶[0507]). No disease or disorder is known to be associated with the claimed polypeptide or encoding nucleic acid. The use of a nucleic acid in an array for screening is only useful in the sense that the information that is gained from the array is dependent on the pattern derived from the array, and says nothing with regard to each individual member of the array. This is a utility which would apply to virtually ever member of a general class of materials, such as any collection of proteins or DNAs. Even if the expression of the claimed nucleic acid is affected by a test compound in an array for drug screening, the specification does not disclose any specific and substantial interpretation for the result, and none is known in the art. Given this

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consideration, the individually claimed nucleic acid has no “well-established” use. The artisan is required to perform further experimentation on the claimed material itself in order to determine to what use any expression information regarding this nucleic acid could be put.

The need to know expression levels instead of relying on vague terms such as “more highly expressed” is illustrated in the following research article: Hu et al. (2003, *Journal of Proteome Research* 2:405-412) analyzed 2286 genes that showed a greater than 1-fold difference in mean expression level between breast cancer samples and normal samples in a microarray (p. 408, middle of right column). Hu et al. discovered that, for genes displaying a 5-fold change or less in tumors compared to normal, there was no evidence of a correlation between altered gene expression and a known role in the disease. However, among genes with a 10-fold or more change in expression level, there was a strong and significant correlation between expression level and a published role in the disease (see discussion section).

Additionally, even if there is upregulation of a gene in a tumor, that tumor is not necessarily vascularized (or, by inference, malignant). Wu et al. (*Gene* 311:105-110, 2003; paragraph bridging col. 1-2 on page 109) report that:

“Interestingly, we observed the up-regulation of BNF-1 not only in breast cancer patients, but also in lung and colon cancer patients, which suggests that the over-expression of BNF-1 is independent of specific tumor type. However, the pathological information provided by commercial companies for these tumor RNAs and cDNAs does not include the vascularized state of the tumor tissues. Therefore, the relationship between the up-regulation of the BNF-1 in tumor tissues and tumor vascularization is not determined in this study.”

If companies providing tumor tissues for expression studies do not supply detailed information about the tumors, then interpretation of expression studies using commercial samples becomes more difficult. It is noted that the “BNF-1” gene of Wu et al. (published after the effective filing date of this application) is identical to the coding region of SEQ ID NO:81 of the instant application. Further, while Wu et al. found overexpression in breast, colon and lung tumors, the instant application apparently did not (Fig. 4).

Another possible utility comes for the finding that the encoding polynucleotide is “more highly expressed” in esophageal or kidney tumors as compared to normal esophagus and kidney tissue (Example 18, p. 142). There is no guidance on how to use this information. No levels (relative or absolute) are disclosed. This information is too sparse to allow the encoding

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polynucleotide to be used as a diagnostic marker for esophageal or kidney tumor. It is not disclosed what type(s) of esophageal or kidney tumor was analyzed. It is not clear if the finding can be generalized to all tumors from that tissue type. The skilled artisan trying to use the results for diagnostic purposes would not know if the results were significant or under what conditions a difference in expression could be detected. It is not clear, for example, if overexpression occurred in 1/10 or 10/10 kidney tumors in pooled sample of 10, with the possibility that extremely high levels from one kidney tumor made levels in a *pooled* sample detectable even though the other nine kidney tumors in the pool had normal levels. Without more specifics about necessary sample size, expression level range for normal and tumor tissues, types of esophageal or kidney tissue that can be used, and other factors, the specification has not provided the invention in a form readily usable by the skilled such that significant further experimentation is unnecessary. Because it is not known if the nucleic acid is involved in causing (or suppressing) the tumor, the skilled artisan could not use it therapeutically as target for treatment of a tumor. It is noted that even if the nucleic acid had utility as a tumor marker, the encoded polypeptide would have no such utility since there is no reason to suspect that there is alteration of polypeptide sequence or amount in esophageal or kidney tumor *versus* normal tissue.

For these reasons, there is no substantial and specific utility for the nucleic acid of SEQ ID NO:81.

Claims 1-20 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

The specification does not provide sufficient guidance or working examples to be able to use the nucleic acid diagnostically or therapeutically, for example in association with esophageal or kidney tumors, to be able to use the claimed invention without undue experimentation. It would require significant further experimentation to be able to use the claimed nucleic acid also because no definite function has been determined for the encoded protein and there is no definite function supported by the prior art.

Claims 1-6, 9, 10 and 14-20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to nucleic acids having at least 80%, 85%, 90%, 95% or 99% sequence identity with a particular disclosed sequence or which hybridizes to a disclosed sequence. The claims do not require that the nucleic acid or encoded polypeptide possess any particular biological activity, nor any particular conserved structure, or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of nucleic acids that is defined only by sequence identity.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form of a recitation of percent identity. There is not even identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. Which nucleic acids of the genus comprising the required sequence are part of the invention has not been set forth.

Other claims are drawn to a nucleic acid encoding specifically the extracellular domain of the polypeptide of SEQ ID NO:82 (with or without its signal sequence), even though no extracellular domain has been described. While a signal peptide was identified as amino acids 1-25 of SEQ ID NO:82 (Fig. 82), the specification does not provide information about if the protein is transported to/through the cell's membrane. Therefore, a nucleic acid encoding an extracellular domain has not been described.

*Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry,

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*whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only isolated nucleic acid comprising the sequence set forth in SEQ ID NO: 81 (or the full-length coding sequence of the cDNA deposited under ATCC 203317) or encoding the polypeptide of SEQ ID NO:82 with or without its signal sequence, but not the full breadth of the claim meets the written description provision of 35 U.S.C. § 112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. § 112 is severable from its enablement provision (see page 1115).

#### ***Claim Rejections - 35 USC § 112, Second Paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6, 9, 10, 14, 15 and dependent claims 7, 8, 11-13, 16 and 17-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-6, 9, 10, 14 and dependent claims are indefinite because of the recitation of "extracellular domain". There has been no extracellular domain identified. While a signal peptide was identified as amino acids 1-25 of SEQ ID NO:82 (see Fig. 82), it is unclear where

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the signal sequence causes the protein to be transported. Accordingly, the limitation that the claimed nucleic acid encodes an “extracellular domain” (for example see claim 1, parts (c) and (d)) is indefinite.

Claims 14 and 15 and dependent claim 16 are also indefinite because the metes and bounds of the claims are not clear. There are no conditions of stringency discussed in claims 14 or 15. It is not clear for claim 14 if non-specific hybridization is included in which structural relatedness is of little consequence. Further, while the skilled artisan understands the general concept of hybridization under “stringent conditions”, what specific conditions are intended by the use of the term “stringent” in claim 15 is unknown. The specification discusses stringent conditions through examples without providing a limiting definition (see ¶[0227]). What conditions of stringency are used in any particular situation are determined by the specificity of hybridization desired by the practitioner. In this case, the desired specificity is unknown. If there is a structural relatedness (limitation) that is being defined by the conditions, then those conditions or range of conditions must be clear in the claim.

### ***35 U.S.C. § 102***

The following rejection under 35 U.S.C. § 102 is made under the assumption that the effective filing date for the instantly claimed invention is 05/08/2002, which is the actual filing date of the instant application. Applicant is advised that the instant application can only receive benefit under 35 U.S.C. § 120 from an earlier application which meets the requirements of 35 U.S.C. § 112, first paragraph, with respect to the new claimed invention. Because the instant application does *not* meet the requirements of 35 U.S.C. § 112, first paragraph, for the reasons given above and it is a continuing application of Serial Number 10/006,867, the prior application also does not meet those requirements for the claimed invention and, therefore, is unavailable under 35 U.S.C. § 120.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

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(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 14-16 are rejected under 35 U.S.C. 102(b) as being anticipated by GenBank Accession AA040433.

GenBank Accession AA040433 teaches a nucleic acid which is 97% identical to SEQ ID NO:81 of the instant application over 381 consecutive bases (see below sequence comparison). This nucleic acid would hybridize according to the limitations of claims 14-16 of the instant application.

Claims 1-10, 12-20 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 200070049.

WO 200070049 teaches the nucleic acid sequence of SEQ ID NO:39 which is 1720 nucleotides long and 100% identical to nucleotides 1-1720 (which includes the full coding region) of SEQ ID NO:81 of the instant application. The encoded protein sequence (SEQ ID NO:18) is identical to SEQ ID NO:82 of the instant application (see below comparison), with the signal sequence designated as amino acids 1-25 (Table 2 of WO). The full-length nucleic acid and vectors and host cells comprising the nucleic acid (p. 53, lines 9-22 and p. 31, line 17- p. 32, line 31) is described. That description includes a nucleic acid encoding a polypeptide lacking its associated signal sequence since disclosed expression in mammalian host cells necessarily is a teaching of production of the encoding protein lacking its signal sequence due to post-translation processing.

AA040433/c **COMPARISON of AA040433 to SEQ ID NO:81**  
LOCUS AA040433 421 bp mRNA linear EST 10-MAY-1997  
DEFINITION zk46c09.s1 Soares\_pregnant\_uterus\_NbHPU Homo sapiens cDNA clone  
IMAGE:485872 3', mRNA sequence.  
ACCESSION AA040433  
VERSION AA040433.1 GI:1516711  
KEYWORDS EST.  
SOURCE Homo sapiens (human)  
ORGANISM Homo sapiens  
Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.  
REFERENCE 1 (bases 1 to 421)  
AUTHORS Hillier,L., Lennon,G., Becker,M., Bonaldo,M.F., Chiapelli,B.,  
Chisoe,S., Dietrich,N., DuBuque,T., Favello,A., Gish,W.,

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Hawkins,M., Hultman,M., Kucaba,T., Lacy,M., Le,M., Le,N.,  
Mardis,E., Moore,B., Morris,M., Parsons,J., Prange,C., Rifkin,L.,  
Rohlfing,T., Schellenberg,K., Soares,M.B., Tan,F., Thierry-Meg,J.,  
Trevaskis,E., Underwood,K., Wohldmann,P., Waterston,R., Wilson,R.  
and Marra,M.

TITLE Generation and analysis of 280,000 human expressed sequence tags  
JOURNAL Genome Res. 6 (9), 807-828 (1996)  
MEDLINE 97044478  
PUBMED 8889549

COMMENT Contact: Wilson RK  
Washington University School of Medicine  
4444 Forest Park Parkway, Box 8501, St. Louis, MO 63108  
Tel: 314 286 1800  
Fax: 314 286 1810  
Email: est@watson.wustl.edu  
This clone is available royalty-free through LLNL ; contact the  
IMAGE Consortium (info@image.llnl.gov) for further information.  
Insert Length: 1346 Std Error: 0.00  
Seq primer: -40M13 fwd. from Amersham  
High quality sequence stop: 341.

FEATURES Location/Qualifiers  
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AACTGGAAGAATTCGCGGCCGCCTTTTTTTTTTTTTTTTTTTT 3'] ,  
double-stranded cDNA was ligated to Eco RI adaptors  
(Pharmacia), digested with Not I and cloned into the Not I  
and Eco RI sites of the modified pT7T3 vector. Library  
went through one round of normalization. Library  
constructed by M. Fatima Bonaldo."

ORIGIN

Query Match 19.8%; Score 343.8; DB 9; Length 421;  
Best Local Similarity 96.9%; Pred. No. 6.3e-47;  
Matches 372; Conservative 0; Mismatches 8; Indels 4; Gaps 2;

Qy 1334 AACCTGCGTCGCTTTGCCCTGGAACAC---GAGGCCTCGGACTTGGTGGAGATCTACCTC 1390  
||||| ||||||||| || || ||||||||| ||||||||| |||||||||  
Db 383 AACCTNCGTGCTTTGCCCTGGAACACNGAGGCCTCGGACTTGGTGGAGATCTACCTC 324

Qy 1391 TGGAAGCTGGTAAAAGATGAGGAAACTGAGGCTCAGAGAGGTGAAGTACCTGGCCCCAAGG 1450  
||||| ||||||||| ||||||||| ||||||||| ||||||||| ||||||||| |||||||||  
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Qy 1451 CCACACAGCCAGAATCTTCCACTTGACTCAGATCAAGAAAGTCAGGAAGCAAGACTTCCA 1510  
||||| ||||||||| ||||||||| ||||||||| ||||||||| ||||||||| |||||||||  
Db 264 CCACACAGCCAGAATCTTCCACTTGACTCAGATCAAGAAAGTCAGGAAGCAAGACTTCCA 205

Qy 1511 GAAAGAGGCACAGCACTTCCGACTGCTCGCTGGCCCCCAGGAAGTCACTGGAACGTCTT 1570  
||||| ||||||||| ||||||||| ||||||||| ||||||||| ||||||||| |||||||||

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Db          204 GAAAGAGGCACAGCACTTCCGACTGCTCGCTGGCCCCACGAAGGTCACTGGAACGTCTT 145

Qy          1571 CCTAGCCCAGACCCTGGAGCTGAAGGTACGGCCAGTCCAGACAAAGTGACCAAGACATA 1630
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          144 CCTAGCCCAGACCCTGGAGCTGAAGGTACGGCCAGTCCAGACAAAGTGACCAAGACATA 85

Qy          1631 ACAAAGACCTAACAGTTGCAGATATGAGCTGTATAATTGTTGTTATTATATATTAATAAA 1690
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          84  ACAAAGACCTAACAGTTGCAGATATGAGCTGTATAATTGTTGTTATTATATATTAATAAA 25

Qy          1691 TAAGAAGTTGCATTACCCTCAAAA 1714
              |||||||||||||||
Db          24  TAAGAAGTTGCATTACCCTCAAAA 1

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**Comparison of WO 200070049 to SEQ ID NO:81 and 82**

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LOCUS      AX048199              1720 bp    DNA        linear    PAT 15-DEC-2000
DEFINITION Sequence 39 from Patent WO0070049.
ACCESSION  AX048199
VERSION    AX048199.1  GI:11876989
KEYWORDS   .
SOURCE     Homo sapiens (human)
  ORGANISM Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE  1
  AUTHORS  Tang, Y.T., Yue, H., Lal, P., Burford, N., Bandman, O., Baughn, M.R.,
            Azimzai, Y., Lu, D.A. and Patterson, C.
  TITLE    Extracellular signaling molecules
  JOURNAL  Patent: WO 0070049-A 39 23-NOV-2000;
            Incyte Genomics, Inc. (US)
FEATURES   Location/Qualifiers
    source  1. .1720
            /organism="Homo sapiens"
            /mol_type="unassigned DNA"
            /db_xref="taxon:9606"
            /note="Incyte ID No: 2267403CB1"
ORIGIN

```

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Query Match          99.3%; Score 1720; DB 6; Length 1720;
Best Local Similarity 100.0%; Pred. No. 0;
Matches 1720; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```

```

Qy=SEQ ID NO:81 1 CCCACGCGTCCGCGCCTCTCCCTTCTGCTGGACCTTCCTTCGTCTCTCCATCTCTCCCTC 60
                  |||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db              1 CCCACGCGTCCGCGCCTCTCCCTTCTGCTGGACCTTCCTTCGTCTCTCCATCTCTCCCTC 60

Qy              61 CTTTCCCCGCGTTCTCTTTCCACCTTTCTCTTCTTCCCACCTTAGACCTCCCTTCCTGCC 120
                  |||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Qy              121 CTCCTTTCTCTGCCCACCGCTGCTTCCTGGCCCTTCTCCGACCCCGCTCTAGCAGCAGACC 180
                  |||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Qy              181 TCCTGGGGTCTGTGGGTTGATCTGTGGCCCTGTGCCTCCGTGTCCTTTTCGTCTCCCTT 240
                  |||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Qy              241 CCTCCCGACTCCGCTCCCGACCGAGCGGCCTGACCTGGGGAAAGGATGGTTCCCGAGGT 300

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Db 241 ||||| CCTCCCGACTCCGCTCCCGGACCAGCGGCCTGACCCTGGGGAAAGGATGGTTCCCGAGGT 300

Qy 301 GAGGGTCCTCTCCTCCTTGCTGGGACTCGCGTGCTCTGGTTCCCCCTGGACTCCCACGC 360

Db 301 ||||| GAGGGTCCTCTCCTCCTTGCTGGGACTCGCGTGCTCTGGTTCCCCCTGGACTCCCACGC 360

Qy 361 TCGAGCCCGCCAGACATGTTCTGCCTTTTCCATGGGAAGAGATACTCCCCGGCGAGAG 420

Db 361 ||||| TCGAGCCCGCCAGACATGTTCTGCCTTTTCCATGGGAAGAGATACTCCCCGGCGAGAG 420

Qy 421 CTGGCACCCCTACTTGGAGCCACAAGGCCTGATGTACTGCCTGCGCTGTACCTGCTCAGA 480

Db 421 ||||| CTGGCACCCCTACTTGGAGCCACAAGGCCTGATGTACTGCCTGCGCTGTACCTGCTCAGA 480

Qy 481 GGGCGCCCATGTGAGTTGTTACCGCCTCCACTGTCCGCCTGTCCACTGCCCCAGCCTGT 540

Db 481 ||||| GGGCGCCCATGTGAGTTGTTACCGCCTCCACTGTCCGCCTGTCCACTGCCCCAGCCTGT 540

Qy 541 GACGGAGCCACAGCAATGCTGTCCCAAGTGTGTGGAACCTCACACTCCCTCTGGACTCCG 600

Db 541 ||||| GACGGAGCCACAGCAATGCTGTCCCAAGTGTGTGGAACCTCACACTCCCTCTGGACTCCG 600

Qy 601 GGCCCCACCAAAGTCCTGCCAGCACAAACGGGACCATGTACCAACACGGAGAGATCTTCAG 660

Db 601 ||||| GGCCCCACCAAAGTCCTGCCAGCACAAACGGGACCATGTACCAACACGGAGAGATCTTCAG 660

Qy 661 TGCCCATGAGCTGTTCCCCTCCCGCCTGCCCAACCAGTGTGTCTCTGCAGCTGCACAGA 720

Db 661 ||||| TGCCCATGAGCTGTTCCCCTCCCGCCTGCCCAACCAGTGTGTCTCTGCAGCTGCACAGA 720

Qy 721 GGGCCAGATCTACTGCGGCCTCACAACTGCCCCGAACCAGGCTGCCAGCACCCCTCCC 780

Db 721 ||||| GGGCCAGATCTACTGCGGCCTCACAACTGCCCCGAACCAGGCTGCCAGCACCCCTCCC 780

Qy 781 ACTGCCAGACTCCTGCTGCCAAGCCTGCAAAGATGAGGCAAGTGAGCAATCGGATGAAGA 840

Db 781 ||||| ACTGCCAGACTCCTGCTGCCAAGCCTGCAAAGATGAGGCAAGTGAGCAATCGGATGAAGA 840

Qy 841 GGACAGTGTGCAGTCGCTCCATGGGGTGAGACATCCTCAGGATCCATGTTCCAGTGATGC 900

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Qy 901 TGGGAGAAAGAGAGGCCCGGGCACCCAGCCCCACTGGCCTCAGCGCCCCTCTGAGCTT 960

Db 901 ||||| TGGGAGAAAGAGAGGCCCGGGCACCCAGCCCCACTGGCCTCAGCGCCCCTCTGAGCTT 960

Qy 961 CATCCCTCGCCACTTCAGACCCAAGGGAGCAGGCAGCACAACTGTCAAGATCGTCCTGAA 1020

Db 961 ||||| CATCCCTCGCCACTTCAGACCCAAGGGAGCAGGCAGCACAACTGTCAAGATCGTCCTGAA 1020

Qy 1021 GGAGAAACATAAGAAAGCCTGTGTGCATGGCGGGAAGACGTACTCCACGGGGAGGTGTG 1080

Db 1021 ||||| GGAGAAACATAAGAAAGCCTGTGTGCATGGCGGGAAGACGTACTCCACGGGGAGGTGTG 1080

Qy 1081 GCACCCGGCCTTCCGTGCCTTCGGCCCCCTTGCCCTGCATCCTATGCACCTGTGAGGATGG 1140

Db 1081 ||||| GCACCCGGCCTTCCGTGCCTTCGGCCCCCTTGCCCTGCATCCTATGCACCTGTGAGGATGG 1140

Qy 1141 CCGCCAGGACTGCCAGCGTGTGACCTGTCCCACCGAGTACCCCTGCCGTACCCCGAGAA 1200

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      |||
Db      1141 CCGCCAGGACTGCCAGCGTGTGACCTGTCCCACCGAGTACCCCTGCCGTACCCCGAGAA 1200
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Db      1201 AGTGGCTGGGAAGTGCTGCAAGATTGCCCAGAGGACAAAGCAGACCCTGGCCACAGTGA 1260
Qy      1261 GATCAGTTCTACCAGGTGTCCCAAGGCACCGGGCCGGGTCCTCGTCCACACATCGGTATC 1320
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Db      1261 GATCAGTTCTACCAGGTGTCCCAAGGCACCGGGCCGGGTCCTCGTCCACACATCGGTATC 1320
Qy      1321 CCCAAGCCCAGACAACCTGCGTCGCTTTGCCCTGGAACACGAGGCCTCGGACTTGGTGGA 1380
      |||
Db      1321 CCCAAGCCCAGACAACCTGCGTCGCTTTGCCCTGGAACACGAGGCCTCGGACTTGGTGGA 1380
Qy      1381 GATCTACCTCTGGAAGCTGGTAAAAGATGAGGAACTGAGGCTCAGAGAGGTGAAGTACC 1440
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Db      1381 GATCTACCTCTGGAAGCTGGTAAAAGATGAGGAACTGAGGCTCAGAGAGGTGAAGTACC 1440
Qy      1441 TGGCCCAAGGCCACACAGCCAGAATCTTCCACTTGACTCAGATCAAGAAAGTCAGGAAGC 1500
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Db      1441 TGGCCCAAGGCCACACAGCCAGAATCTTCCACTTGACTCAGATCAAGAAAGTCAGGAAGC 1500
Qy      1501 AAGACTTCCAGAAAGAGGCACAGCACTTCCGACTGCTCGCTGGCCCCACGAAGGTCACT 1560
      |||
Db      1501 AAGACTTCCAGAAAGAGGCACAGCACTTCCGACTGCTCGCTGGCCCCACGAAGGTCACT 1560
Qy      1561 GGAACGTCTTCCTAGCCCAGACCCTGGAGCTGAAGGTCACGGCCAGTCCAGACAAAGTGA 1620
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Db      1561 GGAACGTCTTCCTAGCCCAGACCCTGGAGCTGAAGGTCACGGCCAGTCCAGACAAAGTGA 1620
Qy      1621 CCAAGACATAACAAAGACCTAACAGTTGCAGATATGAGCTGTATAATTGTTGTTATTATA 1680
      |||
Db      1621 CCAAGACATAACAAAGACCTAACAGTTGCAGATATGAGCTGTATAATTGTTGTTATTATA 1680
Qy      1681 TATTAATAAATAAGAAGTTGCATTACCCTCAAAAAAAAAA 1720
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Db      1681 TATTAATAAATAAGAAGTTGCATTACCCTCAAAAAAAAAA 1720

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Claim 1; Page 90-91; 114pp; English.

Query Match 100.0%; Score 2545; DB 4; Length 451;

Best Local Similarity 100.0%; Pred. No. 3.4e-172;

Matches 451; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy=seq ID NO: 82 1 MVPEVRVLSLLGLALLWFPDLSHARARPMFCLFHGKRYSPGESWHPYLEPQGLMYCLR 60

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Db      1 MVPEVRVLSLLGLALLWFPDLSHARARPMFCLFHGKRYSPGESWHPYLEPQGLMYCLR 60

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Qy 61 CTCSEGAHVSCYRLHCPPVHCPQPVTEPQCCPKCVPHTPSGLRAPPKSCQHNGTMYQH 120

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Db      61 CTCSEGAHVSCYRLHCPPVHCPQPVTEPQCCPKCVPHTPSGLRAPPKSCQHNGTMYQH 120

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Qy 121 GEI FSAHELFP SRLPNQCVLCSCTEGQIYCGLTTCPEPGCPAPLPLPDSGCCQACKDEASE 180

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      |||
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Qy 181 QSDEEDSVQSLHGVRHPQDPCSSDAGRKRGPPTAPTGLSAPLSFI PRHFRPKGAGSTTV 240

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      |||
Db      181 QSDEEDSVQSLHGVRHPQDPCSSDAGRKRGPPTAPTGLSAPLSFI PRHFRPKGAGSTTV 240

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Qy 241 KIVLKEKHKKACVHGGKTYSHGEVWHPAFRAFGPLPCILCTCEDGRQDCQRVTCPTTEYPC 300

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Db      241  KIVLKEKHKKACVHGGKTYSHGEVWHPAFRAFGPLPCILCTCEDGRQDCQRVTCPTTEYPC 300
Qy      301  RHPEKVAGKCKICPEDKADPGHSEISSTRCPKAPGRVLVHTSVSPSPDNLRRFALEHEA 360
Db      301  RHPEKVAGKCKICPEDKADPGHSEISSTRCPKAPGRVLVHTSVSPSPDNLRRFALEHEA 360
Qy      361  SDLVEIYLWKLVKDEETEAQRGEVPGPRPHSQNLPLDSDQESQEARLPERGTLPTARWP 420
Db      361  SDLVEIYLWKLVKDEETEAQRGEVPGPRPHSQNLPLDSDQESQEARLPERGTLPTARWP 420
Qy      421  PRRSLERLPSPDPGAEGHGQSRQSDQDITKT 451
Db      421  PRRSLERLPSPDPGAEGHGQSRQSDQDITKT 451

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### **Conclusion**

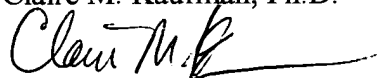
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Claire M. Kaufman, whose telephone number is (571) 272-0873. Dr. Kaufman can generally be reached Monday, Tuesday and Thursday from 8:30AM to 2:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Tony Caputa, can be reached at (571) 272-0829.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Official papers filed by fax should be directed to (703) 872-9306. NOTE: If applicant *does* submit a paper by fax, the original signed copy should be retained by the applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office. **Please** advise the examiner at the telephone number above before facsimile transmission.

Claire M. Kaufman, Ph.D.



Patent Examiner, Art Unit 1646

January 6, 2005

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